REMARKS

Status of the Claims

Claims 1-19 are pending in the application.

Claims 1-13 have been withdrawn from consideration pursuant to 37 C.F.R. §1.142(b).

Claims 14-17 have been amended with entry of this amendment.

Claims 14-19 are currently under consideration with entry of this amendment.

Summary

Claims 1-19 are pending in the application. Claims 1-13 have been withdrawn from consideration pursuant to 37 C.F.R. §1.142(b). Claims 14-19 were examined in the Office Action dated 4 December 2008. In the subject Action, the following claim rejections have been raised: **(a)** claims 14-19 stand rejected under 35 U.S.C. §112, first paragraph on the basis of written description; **(b)** claims 14-19 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite; **(c)** claim 16 stands rejected under 35 U.S.C. §112, second paragraph, as indefinite; **(d)** claims 14-16 stand rejected under 35 U.S.C. §102(b) as unpatentable over Liu et al (1995) *Toxicol. Appl. Pharmacol.* 132:196-202 ("Liu"); **(e)** claims 14-18 stand rejected under 35 U.S.C. §103(a) as unpatentable over Liu in view of U.S. Patent No. 5,039,528 to Olney ("Olney") and in further view of U.S. Patent No. 6,265,379 to Donovan ("Donovan"); **(f)** claims 14-16 stand rejected under 35 U.S.C. §103(a) as unpatentable over Liu in view of Laplanche et al. (2000) *Neuroscience Lett.* 289: 49-52 ("Laplanche"); **(g)** claims 14-15 and 19 stand rejected under 35 U.S.C. §103(a) as unpatentable over U.S. Patent Publication No. 2004/0102525 to Kozachuk ("Kozachuk"); **(h)** claims 14-15 and 19 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 5 of copending US Patent Application No. 10/812,298 ("the '298 Application") in view of Liu; and **(i)** claims 14-16 and 19 stand rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 5 of copending US Patent Application No.

11/226,941 ("the '941 Application") in view of Liu. Applicants respectfully traverse all pending claim rejections for the following reasons.

Overview of the Amendment

Applicants, by way of this amendment, have amended claims 14-17 in order to recite the invention with greater particularity. More specifically, claim 14 has been amended to remove certain functional language objected to by the Office, to recite that administration of the agent is directly to the inner ear, and to recite that the agent is selected from a group consisting of four specified molecules. Support for the amendment to claim 14 can be found throughout the specification as originally filed, and particularly at page 4, line 15. Claim 15 has been amended to recite that administration of the agent is conducted by diffusion across a middle-inner ear membrane. Support for the amendment to claim 15 can be found throughout the specification as originally filed, and particularly at page 12, lines 8-10. Claim 16 has been amended to remove certain language objected to by the Office and to specify that the agent is gacyclidine. Support for the amendment to claim 16 can be found throughout the specification and claims as originally filed, and particularly in original claim 16. Claim 17 has merely been amended to now depend from claim 16. Accordingly, no new matter has been added by way of the amendments to the claims, and the entry thereof is respectfully requested.

The Rejections under 35 U.S.C. §112, First Paragraph

Claims 14-19 stand rejected under 35 U.S.C. §112, first paragraph, on the basis of written description. In particular, the Office has objected that the claim term "agent that modulates glutamate-mediated neurotransmission or sodium channel function" as used in claims 14 and 15, and the claim term "derivatives or analogues thereof" as used in claim 16 lack specificity. Office Action at pages 4-5. In response, applicants draw the Office's attention to the amendments to the claims whereby all of the language objected to by the Office has been deleted. Reconsideration and withdrawal of the rejection of claims 14-197 under U.S.C. §112, first paragraph, is thus earnestly solicited.

The Rejections under 35 U.S.C. §112, Second Paragraph

Claims 14-19 stand rejected under 35 U.S.C. §112, second paragraph, on the basis of indefiniteness. In particular, the Office has objected that use of the expression "significant clinical hearing loss" renders the claims indefinite. Office Action at page 5. Applicants respectfully traverse the rejection for the following reasons.

The fundamental issue regarding compliance with the requirement for definiteness under 35 U.S.C. §112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision. As stated in Section 2173.02 of the MPEP, the relevant inquiry must therefore assess claim language, not in a vacuum, but in light of: (a) the content of applicants' disclosure; (b) the teachings of the prior art; and (c) the claim interpretation that the ordinarily skilled person in the relevant art would give. The mere use of relative language, including terms of degree, does not automatically render the claim indefinite under Section 112, second paragraph. *Seattle Box Co. v. Industrial Crating & Packing, Inc.*, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends instead upon whether or not the skilled person would understand what is claimed, in light of the specification. MPEP §2173.05(b). The term "substantially" is often used in conjunction with other terms to describe a recited invention. Although the term is broad, this is simply insufficient basis to reject a claim since breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 169 USPQ 597 (CCPA 1971). Accordingly, the courts have consistently found that use of the claim term "substantially" is perfectly fine provided that general guidelines have been provided by the specification and/or because one of ordinary art would understand the term. See, e.g., *In re Nehrenberg*, 126 USPQ 383 (CCPA 1960); *In re Mattison*, 184 USPQ 484 (CCPA 1975); and *Andrew Corp. v. Gabriel Electronics*, 6 USPQ2d 2010 (Fed. Cir. 1988).

Applicants have disclosed and claimed methods for treating an inner ear disorder using specified agents that are delivered directly to the inner ear using an administration technique that avoids causing "significant clinical hearing loss." The administration techniques include a number of administration techniques, including surgery in the inner ear. The skilled person is therefore a medically trained physician, specializing in ear,

nose & throat diagnosis and treatment. This is a highly skilled person, having significant post-graduate education, residencies and board certifications. This skilled person is told by applicants' specification that the selected agents for use in the recited methods have significant toxicity issues (bad side effects) that include memory loss, stupor and loss of hearing. However, the conditions that this skilled person is treating include, e.g., tinnitus and other very serious diseases. Tinnitus is characterized by a constant, inescapable ringing or tone in the ear, ranging from a "buzz" or "cricket" sound to an "ocean" or "siren" noise, that causes hearing loss, vertigo, and loss of balance. The condition may sometimes be so severe that sufferers will attempt suicide. Accordingly, applicants instruct the skilled person, a medical practitioner, to administer applicants' recited agents in such a manner as to avoid causing too much damage by the recited side effects. It is absolutely clear to that skilled person that milder conditions will tolerate a much lower rate of hearing loss side effects, whereas much more serious conditions will tolerate a higher degree of hearing loss side effect. Accordingly, the skilled person would understand what "without causing significant clinical hearing loss" means, in light of the teachings provided by applicants' specification, and the medical experience that the practitioner has readily at hand. For all of the foregoing reasons, then, applicants submit that the rejection of the claims on the basis of use of the term "significant" is improper. Reconsideration and withdrawal of the rejection of claims 14-19 under U.S.C. §112, second paragraph, is thus earnestly solicited.

Claim 16 stands rejected under 35 U.S.C. §112, second paragraph, on the basis of indefiniteness. In particular, the Office has objected that use of the expression "derivatives or analogues thereof" render the claims indefinite. Office Action at page 6. In response, applicants draw the Office's attention to the amendment to claim 16 whereby the subject language has been deleted from the claim. Reconsideration and withdrawal of the rejection of claim 16 under U.S.C. §112, second paragraph, is thus earnestly solicited.

The Rejection under 35 U.S.C. §102

Claims 14-16 stand rejected under 35 U.S.C. §102(b) as unpatentable over Liu. In particular, the Office asserts that Liu "teaches the protective effect of MK-801 against carbon monoxide-induced hearing loss." Office Action at page 7. Applicants respectfully traverse the rejection.

Initially, applicants draw the Office's attention to its' Requirement for Species Election dated 14 October 2008, whereby each NMDA receptor antagonist has been made an independent or distinct single species. Applicants elected the species of gacyclidine in their Response dated 6 November 2008, and the Office made the Requirement for Election final with the present Office Action (see pages 2 and 3 of the Office Action). Accordingly, applicants are prosecuting the elected invention of methods for administering the gacyclidine agent to the inner ear.

As noted by the Office, Liu teaches use of a non-elected species, MK-801. The MPEP instructs that the criteria for a proper requirement for restriction between patentably distinct inventions require that the inventions "must be independent or distinct". MPEP §803. Since applicants have disclosed that their various recited NMDA receptor antagonists are related by activity, the Office must have taken the position that methods for administering each recited NMDA receptor antagonist are distinct ("where restriction is required by the Office ... it is imperative the requirement should never be made where related inventions as claimed are not distinct" MPEP §806). Related inventions are distinct only if they are not connected in at least one of design, operation or effect ... and wherein they are PATENTABLE (novel and nonobvious) OVER EACH OTHER. MPEP §802.01.

Accordingly, the Offices position that a patentably distinct, non-elected species (use of MK-801) somehow destroys the novelty of applicants' elected novel and nonobvious species (use of gacyclidine) must be improper. Reconsideration and withdrawal of the rejection of claims 14-16 under 35 U.S.C. §102(b) is thus earnestly solicited.

The Rejections under 35 U.S.C. §103

Claims 14-18 stand rejected under 35 U.S.C. §103(a) as unpatentable over Liu in view of Olney, and in further view of Donovan. In particular, the Office asserts "Liu teaches the protective effect of the NMDA antagonist MK-801 against carbon monoxide-induced hearing loss ... [and Olney] teaches the administration of NMDA antagonist D-AP5." Office Action at page 8. The Office concludes "it would have been obvious .... To administer the NMDA antagonist MK-801 to the inner ear through the round window membrane ... as taught by Liu for a period lasting until full protection has been achieved." Office Action at page 9. Finally, the Office recites Donovan as teaching that "tinnitus, particularly inner ear tinnitus is due to cochlear nerve dysfunction [and] that local administration for the treatment of tinnitus includes injection." Office Action at page 9. Applicants respectfully traverse the rejection for the following reasons.

Here again applicants remind the Office that it has taken the position that methods for administration of the NMDA antagonists MK-801 and D-AP5 are patentably distinct (novel and nonobvious) over each other, and are further patentably distinct (novel and nonobvious) from applicants' elected species that is drawn to methods for administration of gacyclidine. Accordingly, the rejection of claims 14-16 over the combination of Liu, Olney and Donovan must be improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 14-16 stand rejected under 35 U.S.C. §103(a) as unpatentable over Liu in view of Laplanche. In particular, the Offices cites the primary reference to Liu as teaching the protective effect of the NMDA antagonist MK-801 against carbon monoxide-induced hearing loss. The Office then cites the secondary reference to Laplanche as teaching that both MK-801 and gacyclidine have toxicity side effects. Office Action at page 10. Applicants respectfully traverse the rejection for the following reasons.

Here again applicants remind the Office that it has taken the position that methods for administration of the NMDA antagonist MK-801 is patentably distinct (novel and nonobvious) over methods for administration of gacyclidine. Accordingly, the Office's proposed combination of references must be improper, and the rejection of claims 14-16

over the combination of Liu and Laplanche must also be improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 14-15 and 19 stand rejected under 35 U.S.C. §103(a) as unpatentable over Kozachuk. In particular, the Office asserts that Kozachuk "discloses the use of the NMDA antagonist memantine for the treatment of tinnitus." Office Action at page 11.

Here again applicants remind the Office that it has taken the position that methods for administration of the NMDA antagonist memantine is patentably distinct (novel and nonobvious) over methods for administration of gacyclidine. Accordingly, the Office's rejection of claims 14-15 and19 over Kozachuk must be improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

The Obvious-Type Double Patenting Rejections

The following provisional rejections have been raised:

- claims 14-15 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 5 of the '298 Application in view of Liu; and

- claims 14-16 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1 and 5 of the '941 Application in view of Liu.

Applicants respectfully traverse the provisional rejections. Applicants further request that all provisional rejections be held in abeyance until allowable subject matter has been determined in the present application.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a

telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

The appropriate fee is either attached or authorized. If the Commissioner determines that an additional fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953.**

Respectfully submitted,

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